A Rare case of HUS and ADEM

A 3-year-old girl was admitted with typical hemolytic uremic syndrome (HUS) and conservative treatments were initiated. During hospitalization, she had seizures, right hemiparesis, and loss of consciousness. Initial MR of the brain showed changes of acute disseminated encephalomyelitis (ADEM). She was treated with intravenous methylprednisolone and immunoglobulin. Upon improvement of her clinical condition, she was discharged with oral prednisolone which was tapered after two months. After one year follow-up, the child now has a normal renal function and normal neurodevelopment.

Keywords: Hemolytic-Uremic syndrome; Hematuria; Acute Disseminated Encephalomyelitis; Child.

Introduction

A decreased platelet count is found in all types of HUS but it is temporary and variable. Microangiopathic hemolytic anemia (MAHA) is a Coombs negative hemolytic anemia. Fragmented erythrocytes (schistocytes) are seen on the peripheral blood smear. The plasma level of lactate dehydrogenase is elevated but haptoglobin is reduced. Assessment of serum haptoglobin is a very sensitive test of intravascular hemolysis. It is the last parameter to return to normal when MAHA resolves. There is no correlation between the severity of MAHA and clinical outcome. When HUS occurs after an infection, the renal failure will appear suddenly and is typically oligoanuric. All types of HUS have proteinuria. If there is complement disregulation, blood pressure elevation is usually severe at onset and difficult to control. Patients with infection induced HUS usually have normal or only mildly elevated blood pressure at first but during the recovery period of oliguric renal failure, they experience a transient hypertension. Most of the cases of childhood HUS (over 90%) occur following intestinal E Coli infection due to its Shiga toxin. There is typically bloody diarrhea followed by HUS in children over 6 months of age. Other cases of HUS occur following severe streptococcal pneumonia infection as empyema, pneumonia, meningitis, or rarely septicemia [1]. If there is hereditary predisposition to HUS, the disease presents with an insidious onset, pallor, lethargy, and feeding discomfort but the prodromal diarrhea may be absent. There may be severe hypertension and family history of HUS. In these cases, there may be mutations in complement regulators and, less often, an inherited deficiency of von Willebrand factor or a hereditary error of cobalamin metabolism. There is a small group of HUS cases in whom the cause is not detected in spite of full investigations, even suspected drug effects, cancer, or bone marrow transplant. They are less than 5% of all childhood HUS cases and most of them have only one attack with usually good
recovery of the renal function, and the prognosis appears to be favorable [2]. One of the rare neurological diseases is acute disseminated encephalomyelitis (ADEM), which occurs in children more than adults. It seems that ADEM is a monophasic inflammatory demyelinating condition with clinical manifestations including encephalopathy, and focal or multifocal neurologic syndromes due to a central nervous system (CNS) inflammatory disorder. In this condition, especially in children, prolonged and severe headaches occur along with fever. The clinical presentation of ADEM may be similar to other inflammatory demyelinating disorders, especially multiple sclerosis (MS) and neuromyelitis optica; therefore, it is important to distinct it for determining the prognosis and treatment planning [3]. Over 50% of the patients have a history of an illness, usually an infection, two to four weeks before developing ADEM. Most of these illnesses are very mild and brief viral or bacterial infections like an upper respiratory tract infection. The neurologic symptoms include confusion, drowsiness, coma, disequilibrium, unsteadiness, and even falling down, visual blurring or diplopia (occasionally), swallowing difficulties, and weakness of the upper or lower limbs. Few reports indicate that ADEM occurs three months or less following measles, mumps, and rubella vaccination. There is a marked increase in signal intensity throughout the white matter in T2-weighted MRI of ADEM patients, which affects corpus callosum and periventricular region commonly [4]. However, these lesions may resolve soon and often in the weeks that follow. The CSF is frequently normal but abnormalities like mild lymphocytic pleocytosis and increased protein concentrations may be detected. High-dose IV methylprednisolone therapy is helpful in approximately 50% of the cases but in refractory cases, intravenous immunoglobulin and plasma exchange may be beneficial. However, there is no standard treatment protocol yet.

Case Report
Our case was a 3-year-old girl with fever and gastroenteritis. At first, she was conscious but severely ill and dehydrated. Laboratory findings showed anemia, thrombocytopenia, an elevated reticulocyte count, and a high lactic dehydrogenase (LDH) level, as well as schistocytosis and spherocytosis in the peripheral blood smear. The Coombs test was negative. She was oliguric at first but became anuric subsequently. The stool examination was insignificant and the stool culture was unremarkable. She was managed as a case of HUS syndrome. The primary medical care consisted of replacement of fluid and electrolytes, peritoneal dialysis, and antihypertensive drugs for her mild hypertension. Afterwards, her condition became better with an acceptable urine output per hour. Blood pressure and serum BUN, Cr, reticulocyte count and LDH levels returned to normal soon. However, in the course of hospitalization, bloody diarrhea, high grade fever and severe hypertension were added to her clinical symptoms and she experienced status epilepticus. Then, she lost her full consciousness and developed right hemiparesis and aphasia and lost her insight to people around her. Serum complements, factor H, I, F, ADAMTS 13 and antibodies were normal. Brain MRI demonstrated periventricular demyelination (compatible with ADEM). She received intravenous immunoglobulin (IVIG) and methylprednisolone plus other therapies and at the same time, serum complements and factors H, I, F and serum ADAMTS 13 antibody levels were checked repeatedly. As she improved and initial problems disappeared, she was discharged with oral prednisolone and followed up as an outpatient. Then, the oral corticosteroid dose was tapered after two months of therapy in conjunction with neurological function improvement. After 18 months of outpatient therapy, she had normal urine flow and renal function and no other episodes of seizure or any other neurological disruption occurred. All drugs were then discontinued.

Discussion
We describe a 3-year-old girl with typical HUS that was followed by CNS involvement presenting as
fever, seizure, and hemiparesia. Brain MRI findings and CNS involvement suggested ADEM syndrome. There are no accepted or pathologically verified clinical diagnostic criteria for ADEM. The occurrence of acute symptoms (more than one neurological deficit) in a previously healthy child, any change in the mental state, or any combination of alterations seen on MRI providing that they included white matter lesions, were considered as ADEM syndrome [3]. More than half of the patients have an illness, usually an infection, two to four weeks before developing ADEM. However, there is no report of ADEM after HUS in the literature. After the manifestation of neurologic deficits, seizure, and fever in our patient, we suspected atypical HUS and evaluated complements and factors H, I, F, and Adams 13 antibodies, which were all normal.

It seems that ADEM is an immune reaction following an infectious attack which targets the central nervous system instead of infection and causes inflammatory changes in it. There is demyelination of neurid tissues in ADEM, too [5]. The cause-and-effect relationship between viral infection and many post infection syndromes is impossible to establish, especially when there is a 30-day latency period between the viral infection and the onset of neurological dysfunction. There is at least four to six viral illnesses each year in a school age child, so approximately half or more of the children have a viral illness 30 days before the onset of any life event. This probability is higher for preschool-aged children in day care centers. Lethargy, headache, and vomiting are common presentations of encephalopathy but these systemic features may be symptoms of a viral illness as well. Neurological symptoms often present abruptly and are characterize by focal motor signs or altered states of consciousness, or both. In some children, focal neurological signs do not appear while in others, the initial presentation suggests a focal mass effect. In the first week, the risk of mortality is the highest and a favorable outcome is not the rule. Many children with ADEM syndrome have repeated episodes, a course similar to that of multiple sclerosis [6]. Our case developed ADEM secondary to probably an intestinal bacterial infection but unfortunately, we could not detect any microorganisms in her stool sample. However, CNS vasculitis due to HUS itself could be a cause of ADEM in our patient.

Conflict of Interest
None declared

Financial Support
None declared

References